of sample employed to produce the kinetic measurements. Generally, eight points (plus initial sample) taken during at least 2 half-lives were obtained. For each sample relative concentration of product at each time period was obtained by integrating the product peak and dividing that value by the integration value obtained for the internal standard peak. The slope of the linear regression analysis of ln concentration vs. time afforded the pseudo-first-order rate constant.

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Registry No. I, 116-06-3; II, 1646-75-9; VI, 98800-47-6; $Cu(NO_3)_2$, 3251-23-8; $ZnCl_2$, 7646-85-7.

Reactions of *N*-Halobenzylalkylamines with Sodium Methoxide in Methanol

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Reactions of *N*-halobenzylmethylamines 1 and 2 (X = Cl and Br) with MeONa–MeOH have been investigated. Eliminations from 1 were quantitative, producing only benzylidenemethylamines. Reaction of 2 with MeONa–MeOH produced benzylidenemethylamines and benzylmethylamines. The yield of benzylidenemethylamine increased with electron-withdrawing aryl substituents and increased base concentration and became quantitative when pentane was used as a solvent. The results are interpreted as competing bimolecular elimination and nucleophilic substitution by methoxide on bromine. Product studies for reaction of *N*-halobenzyl-*tert*-butylamines with MeONa–MeOH and EtSNa–MeOH establish that the substitution reaction is a general reaction pathway available for the *N*-haloamines. Transition states for eliminations from 1 and 2 are characterized by Hammett ρ and primary deuterium isotope effect values.

Base-promoted, alkene-forming reactions have been extensively investigated, and a rather detailed understanding of steric and electronic effects in these reactions has evolved.[2a,3a] In contrast, relatively little is known about the influence of such factors in base-promoted eliminations which form carbon–nitrogen double bonds.[2b,4-11]

Unexpectedly large differences in E2 transition-state structures for base-promoted, imine-forming eliminations from $ArCH_2N(X)R$ compounds have been reported. When the leaving group was chlorine and the base–solvent combination was MeONa–MeOH or *t*-BuOK–*t*-BuOH, E2-central type of transition states were evident with appreciable C_β–H and N_α–Cl bond cleavage and significant double bond character.[8] On the other hand, for arenesulfonate leaving groups and amine bases in H_2O–THF–EtOAc or MeOH, the transition states are E1-like with extensive N_α–OSO_2Ar bond rupture but limited C_β–H bond scission and carbon–nitrogen double bond development.[9-11] At this stage it is not possible to deduce whether these transition-state differences result from the replacement of a poorer (chloride) leaving group by a better one (arenesulfonate)[10] or a variation in strength and charge type of the base or a combination of these two factors. To assess the influence of a change to a better leaving group with a constant base–solvent combination, we have investigated reactions of *N*-chlorobenzylmethylamines **1a–e** and *N*-bromobenzylmethylamines **2a–e** with MeONa–MeOH under the same experimental conditions. It should be noted that bromide is an even better leaving group than

Table I. Rate Coefficients for Eliminations from $ArCH_2N(Cl)CH_3$ Promoted by MeONa–MeOH

entry	compd[a]	temp, °C	[MeONa], M	$10^2k_2^E$,[b] M^{-1} s^{-1}
1	**1a**	25.0	0.0172	1.06
2	**1a**	25.0	0.172	1.13
3	**1b**	25.0	0.172	0.177
4	**1a**	35.0	0.172	2.41
5	**1a**	45.0	0.172	5.42
6	**1c**	25.0	0.172	0.568
7	**1d**	25.0	0.172	5.29
8	**1e**	25.0	0.172	21.1

[a] [Substrate] = 3.0–8.5 × 10^{-5}. [b] Estimated uncertainty, ±3%.

Table II. Effect of Aryl Substituents upon Yields of Elimination Products from Reactions of $YC_6H_4CH_2N(Br)CH_3$ with 0.0172 M MeONa–MeOH at 25.0 °C

Y	yield of **3**,[a] %
p-CH_3O	56.5
H	81.2
m-Br	87.2
m-NO_2	98.2

[a] Estimated uncertainty, ±1%.

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Table III. Effect of Base Concentration and Solvent upon the Yield of Elimination Product from Reaction of p-$CH_3OC_6H_4CH_2N(Br)CH_3$ with MeONa

[MeONa],[a] M	yield of 3,[c] %
0.0172	56.3
0.100	76.4
1.00	88.9
1.72	100
MeONa–pentane	100

[a] Methanol was used as a solvent except as otherwise noted. [b] Heterogeneous mixture. [c] Estimated uncertainty, ±1%.

tosylate for eliminations from $ArCH_2CH_2X$ promoted by EtONa–EtOH.[12]

$$YC_6H_4CL_2N(X)CH_3 + MeONa\text{–}MeOH \rightarrow \underset{1,\ X = Cl}{\underset{2,\ X = Br}{YC_6H_4CL{=}NCH_3}} + \underset{4}{YC_6H_4CL_2NHCH_3} \quad (1)$$

$$\underset{3}{}$$

a, Y = H; L = H

b, Y = H; L = D

c, Y = p-CH_3O; L = H

d, Y = m-Br; L = H

e, Y = m-NO_2; L = H

Results

Reactions of **1** with MeONa–MeOH yielded only the benzylidenemethylamines **3**. Eliminations were followed by monitoring the appearance of absorption at the λ_{max} for **3**. Pseudo-first-order conditions (base in at least 10-fold excess) were employed. Excellent pseudo-first-order kinetic plots which covered at least two half-lives were obtained. Dividing the pseudo-first-order rate constants by the base concentrations provided the second-order rate coefficients recorded in Table I.

Reactions of **2** with MeONa–MeOH produced both the benzylidenemethylamines **3** and the corresponding benzylmethylamines **4**. The proportion of elimination product increased with the electron-withdrawing power of the aryl group substituent in **2** (Table II). In addition, the proportion of elimination product **3c** formed in reaction of **2c** with MeONa–MeOH increased as the concentration of MeONa was enhanced (Table III). Quantitative formation of **3c** was observed with 1.72 M MeONa–MeOH and with MeONa–pentane.

Kinetics for the reactions of **2** with MeONa–MeOH were followed in the same fashion as for **1** and rate coefficients were calculated similarly with the exception that the overall second-order rate constants, k_2, were multiplied by the imine yield to afford the second-order rate constant for imine formation, k_2^E. The k_2 and k_2^E values are presented in Table IV.

Both **1** and **2** were found to be stable in MeOH for periods of time similar to those used for the base-promoted elimination reactions.

The rate coefficients which appear in Tables I and IV provide ample evidence that the elimintions from **1** and **2** are first order in base as well as first order in substrates. Second-order rate coefficients for reactions of **1a** with MeONa–MeOH are constant for a 10-fold variation in base concentration (entries 1 and 2, Table I). Similarly the k_2^E values for reactions of **2a** are constant for a 100-fold variation in base concentration (entries 1–4, Table IV).

Rates of elimination from **1a** and **2a** promoted by MeONa–MeOH were measured at three temperatures spanning 20 °C. Arrhenius plots exhibited excellent linearity. Calculated enthalpies and entropies of activation are presented in Table V.

From the rate coefficients for eliminations from **1a** and **2a** and their deuterated analogues, **1b** and **2b**, primary deuterium isotope effect values were calculated and are also listed in Table V.

The influence of aryl group substituents upon elimination rates from **1** and **2** correlated satisfactorily with Hammett σ^- values. Hammett ρ values are recorded in Table V.

To better understand the competitive formation of benzylmethylamines **4** in reactions of **2** with MeONa–MeOH, reactions of *N*-halobenzyl-*tert*-butylamines with MeONa and EtSNa in MeOH were briefly examined. From reactions of *N*-bromobenzyl-*tert*-butylamine (**5**) with 1.14 M MeONa–MeOH at room temperature both benzylidene-*tert*-butylamine and benzyl-*tert*-butylamine were obtained in yields of 26.5% and 73.5%, respectively. The proportion of elimination product from **2a** was determined to be 92.6% under the same conditions. Upon reaction with 1.14 M MeONa–MeOH, *N*-chlorobenzyl-*tert*-butylamine (**6**) produced only benzylidene-*tert*-butylamine, but a quantitative yield of benzyl-*tert*-butylamine was realized upon reaction with 1.14 M EtSNa–MeOH.

Discussion

Effect of Leaving Group in Imine-Forming Elimination Reactions. The kinetic investigation and control experiments clearly establish that formation of **3** by MeONa–MeOH promoted eliminations from **1** and **2** proceed via an E2 mechanism. Since **1** and **2** were found to be stable in MeOH, solvolytic elimination is demonstrated to be unimportant. In addition, the observed second-order kinetics, first order in substrate and first order in base, rule out all but bimolecular reaction pathways. An E1cB mechanism is negated by substantial values of the primary deuterium isotope effect (Table V) and the element effect of the leaving group.

For eliminations from **1a** and **2a** induced by MeONa–MeOH the entropies of activation (Table V) are the same within experimental error. Thus the moderate rate enhancement produced by the leaving group variation (k_{Br}/k_{Cl} = 15.8) results from enthalpic factors.

Positive ρ values for the base-promoted eliminations of **1** and **2** promoted by MeONa–MeOH (Table V) attest to development of negative charge on the benzylic carbon in the transition states. As the leaving group is changed from chlorine to bromine, the ρ value decreases from 1.73 to 1.60. Thus the carbanionic character at C_β diminishes as the leaving group becomes better.

The primary deuterium isotope effect indicates the extent to which the benzylic proton is transferred to the base in the transition state.[13] For both the dehydrochlorination of **1a** and the dehydrobromination of **1b**, a large k_H/k_D value of 6.4 indicates considerable C_β–H bond rupture in the transition state. Apparent invarience in the k_H/k_D value with change in leaving group could result from the double-valued nature of the primary deuterium isotope effect[13] or from insensitivity of this mechanistic probe to the structural variation. In view of the change in ρ values noted when chlorine is replaced by bromine as the leaving group, the former explanation is favored.

The Hammett ρ and k_H/k_D values of 1.60 and 6.4, respectively, observed for eliminations from **2** in this study, contrast sharply with those reported for related eliminations in which arenesulfonate is the leaving group and the

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Table IV. Rate Coefficients for Reactions of $ArCH_2N(Br)CH_3$ with MeONa–MeOH

entry	compd[a]	temp, °C	[MeONa], M	k_2,[b] M^{-1} s^{-1}	yield of 3, %	k_2^E,[c,d] M^{-1} s^{-1}
1	**2a**	25.0	0.172	0.183	89.3	0.163
2	**2a**	25.0	0.100	0.194	88.2	0.171
3	**2a**	25.0	0.0172	0.209	81.2	0.170
4	**2a**	25.0	0.00172	0.248	66.5	0.165, 0.167[e]
5	**2a**	35.0	0.0172	0.623	62.9	0.391, 0.391[e]
6	**2a**	45.0	0.0172	1.490	55.0	0.819, 0.819[e]
7	**2b**	25.0	0.700	0.0492	53.1	0.0261
8	**2b**	25.0	0.350	0.0528	49.8	0.0262, 0.0262[e]
9	**2c**	25.0	0.172	0.0955	83.9	0.0799
10	**2c**	25.0	0.100	0.110	76.4	0.0840, 0.0819[e]
11	**2d**	25.0	0.0172	0.965	87.2	0.841
12	**2d**	25.0	0.0130	1.00	80.3	0.803, 0.822[e]
13	**2e**	25.0	0.00500	2.88	79.2	2.28
14	**2e**	25.0	0.00350	3.04	75.2	2.29, 2.29[e]

[a] [Substrate] = 5.0–8.5 × 10^{-5} M. [b] $k_2 = k_{obsd}/[MeONa]$. [c] $k_2^E = k_2 \times$ imine yield. [d] Estimated uncertainty, ±3%. [e] Average value.

Table V. Transition-State Parameters for Eliminations from *N*-Halobenzylmethylamines Promoted by MeONa–MeOH

compd	benzylic ρ	k_H/k_D	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
$ArCH_2N(Cl)CH_3$	1.73 (r^a = 0.999)	6.4[b]	14.9[b]	−16.8[b]
$ArCH_2N(Br)CH_3$	1.60 (r^a = 0.999)	6.4[b]	13.7[c]	−16.1[c]

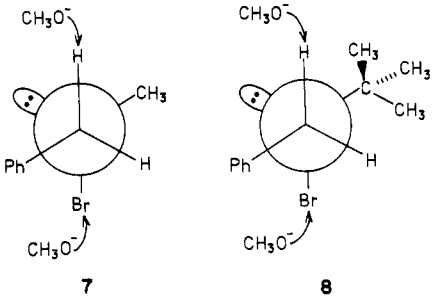
[a] Correlation coefficient. [b] For **1a**. [c] For **2a**.

base is an amine. For benzylamine-promoted eliminations from $ArCH_2NHOSO_2C_6H_4$-*m*-CF_3 in MeOH,[11] ρ = 0.11 (0.32 when the base was pyrrolidine) and k_H/k_D = 1.2. Anticipating similar leaving group propensities for bromide and arenesulfonate,[12] it appears that the striking differences in transition-state characters for these two systems result primarily from the change in base strength and charge type. According to the tenets of the Variable E2 Transition State Theory,[2c] change from a stronger base to a weaker one should decrease the extent of C_β–H bond rupture in the transition state which would be reflected in lower ρ and k_H/k_D values, as observed. It should be noted that amines are generally of insufficient basicity to promote alkene-forming elimination reactions. However, the greater facility of eliminations that form carbon–nitrogen double bonds markedly expands the variety of bases which may be utilized.

Nucleophilic Substitution at Halogens of *N*-Halobenzylmethylamines. Reactions of **2** with MeONa–MeOH produce the corresponding benzylmethylamines **4** as well as the elimination product **3**. Since the absence of unimolecular, solvolytic processes was demonstrated, the formation of both products may be rationalized as competing bimolecular elimination and nucleophilic substitution at halogen.[14]

The yield data contained in Table II support this contention. In reactions of **2** with MeONa–MeOH the yield of elimination product systematically increases as the electron-withdrawing ability of the aryl substituent is enhanced. Increased electron withdrawal by an aryl ring substituent would be predicted to have a larger influence upon the benzylic hydrogen acidity than upon the leaving group ability of the more distant nitrogen atom.[15] Therefore an enhanced proportion of elimination product is predicted in accord with the observed yields.

To further explore the competition between elimination and substitution, products were determined for reactions of *N*-bromobenzyl-*tert*-butylamine (**5**) and **2a** with 1.14 M MeONa–MeOH. The former yielded 26.5% elimination and 73.5% substitution, whereas **2a** produced 92.6% elimination and 7.4% substitution. These results may be readily rationalized by consideration of structures **7** and



7 **8**

8. Compared with **2a** (structure **7**) base attack on the benzylic hydrogen of **5** is sterically hindered by the *N*-*t*-Bu group (structure **8**). On the other hand, steric requirements for nucleophilic substitution at bromine is very similar for both substrates. Therefore the relative proportion of elimination product should be greater from **2a** (structure **7**) than **5** (structure **8**).

To determine if the substitution reaction is unique to *N*-bromoamines, products from reactions of *N*-chlorobenzyl-*tert*-butylamine (**6**) with MeONa and EtSNa in MeOH were determined. Reaction of **6** with 1.14 M MeONa–MeOH produced the elimination product in quantitative yield. However, reaction of **6** with 1.14 M EtSNa–MeOH formed only benzyl-*tert*-butylamine. This complete change of reaction pathway may be rationalized according to the hardness of the attacking base; i.e., the hard base attacks the benzylic hydrogen and the soft base attacks chlorine.[16] The observation of substitution products from reactions of **2**, **5**, and **6** suggests that nucleophilic attack on halogen is a general reaction pathway for *N*-haloamines.

Very recently a study of nucleophilic displacement of chlorine from *N*-chloroacetanilides by triethylamine was reported.[14] In comparison, expulsion of a poorer nitrogen leaving group for substitution reactions of *N*-haloamines might be expected to provide some difficulty. Support for this expectation may be found in the data presented in Table III. For reaction of **2c** with MeONa–MeOH, the proportion of elimination product increased with base concentration enhancement and became quantitative at high base concentration and in pentane. This result may be rationalized if cleavage of the nitrogen leaving group is catalyzed by free methanol. Increasing the base concentration would decrease the concentration of free methanol available for the substitution reaction. Therefore, the substitution reaction would be supressed at high

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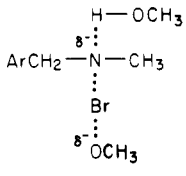
base concentration and be negligible in an aprotic solvent.

Rate data contained in Table IV are also consistent with this interpretation. If the substitution reaction is catalyzed by free methanol, the second-order rate constants for the substitution reaction, k_2^S, would be expected to decrease with increasing MeONa concentration (vide supra). On the other hand, those for the elimination reaction, k_2^E, should remain constant. In agreement, the k_2^E values are invariant but the overall second-order rate coefficients ($k_2 = k_2^S + k_2^E$) decrease with increasing base concentration. Therefore, the transition-state structure for attack of methoxide at bromine in **2** is envisioned as **9** in which a hydrogen-bonded methanol molecule helps to stabilize the developing negative charge on nitrogen.



9

Experimental Section

Benzylidenemethylamines **3**, benzylmethylamines **4**, and *N*-halobenzylmethylamines **1** and **2** and MeONa–MeOH were prepared as described previously.[8] Benzylidene-*tert*-butylamine, benzyl-*tert*-butylamine, *N*-bromobenzyl-*tert*-butylamine (**5**) and *N*-chlorobenzyl-*tert*-butylamine (**6**) were prepared by known methods.[8,17]

Products from reactions of **1** and **2** with MeONa–MeOH were isolated and identified as before.[8] Yields of **3** from reactions of **2** with MeONa–MeOH were determined by comparing the UV absorbances of the reaction products with those for authentic samples.

Reactions of *N*-chloro- and *N*-bromobenzyl-*tert*-butylamines (**6** and **5**, respectively) with MeONa–MeOH were carried out by stirring the solution of **6** or **5** in MeOH (7.26×10^{-2} M, 3.0 mL), MeONa–MeOH (2.28 M, 3.0 mL), and *tert*-butylbenzene (internal standard, 0.2 mmol) for 12 h at room temperature. The solvent was removed in vacuo, and the residue was extracted with diethyl ether and analyzed by gas chromatography on a 20-m Carbowax 20M capillary column with temperature programming from 110–200 °C. The products were benzylidene-*tert*-butylamine (99.5%) from **6** and benzylidene-*tert*-butylamine (26.5%) and benzyl-*tert*-butylamine (73.5%) from **5**, respectively.

The reaction of **6** with EtSNa–MeOH was carried out by the same procedure except that the EtSNa–MeOH was prepared by adding EtSH (13.5 mmol) to MeONa–MeOH (2.28 M, 3.0 mL). In this reaction, benzyl-*tert*-butylamine was obtained in 99.8% yield.

Stability of the *N*-haloamines in MeOH was demonstrated by the previously used method.[8]

Kinetic studies were carried out as before[8] using a Cary 17D UV spectrophotometer. The pseudo-first-order rate constant was divided by the base concentration to afford the second-order rate constant, k_2. For reaction of **2** with MeONa–MeOH, the k_2 values were multiplied by the imine yields to obtain the second-order rate constant for imine formation, k_2^E.

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Registry No. **1a**, 3555-71-3; **1c**, 70972-89-3; **1d**, 70972-94-0; **1e**, 70972-96-2; **2a**, 98760-21-5; **2c**, 98760-20-4; **2d**, 98760-22-6; **2e**, 98760-23-7; **3a**, 622-29-7; **3c**, 13114-23-3; **3d**, 35003-56-6; **3e**, 877-80-5; **4a**, 103-67-3; **4c**, 702-24-9; **4d**, 67344-77-8; **5**, 98777-15-2; **6**, 33863-73-9; PhCH=NBu-*t*, 6852-58-0; $PhCH_2NHBu$-*t*, 3378-72-1.

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Highly Regioselective Ring Cleavage of *N*-Acylaziridines by "Anthracene Hydride" (Anion of 9,10-Dihydroanthracene). Intermediacy of a Carbonyl Adduct. Influence of Nitrogen Inversion on the Ring Opening?[1,2]

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Anthracene hydride AH^- reacts with *N*-acylaziridines by reductive opening of the aziridine ring and/or amidoethylation of AH^-. When the two aziridine carbons are differently substituted, in both reactions only that bond is broken which can form the more stable carbon radical quite in accord with the intermediacy of a radical anion (ketyl) **14** and with the known homolytic cleavage of **14** forming the radical **15**. The extra electron in **14** is provided by AH^- being oxidized to the radical AH·, which can react with **15** either by radical combination or by hydrogen transfer. The reaction of AH^- with *N*-aroylaziridines can be interrupted at the stage of the carbonyl adduct **5** as is shown by the isolation of the ketones **7a,b**. So, **5** (R^4 = aryl) is considered to be in equilibrium with the radical pair AH·/**14**. The conversion of **5** into the final products progresses as expected from its structure apart from the observed retardation by a phenyl substituent in the aziridine ring (**3a**, **4a**). This retardation is tentatively explained by a hypothesis assuming ring opening of **14** to occur in the transition state of nitrogen inversion. The anion X^- of xanthene resembles AH^- in its reactivity. Both carbanions react with *N*-sulfonylaziridines as expected from an S_N2 mechanism.

The anions of dihydroarenes are formally composed of the corresponding arene and a hydride ion. They may therefore be called arene hydrides for convenience. Since they are negatively charged analogues of dihydropyridines,

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